OPEN ACCESS Freely available online

ISSN: 2155-9589
Journal of Membrane Science & Technology

Perspective

The Role of Basement Membrane Mechanics in Health and Disease

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DESCRIPTION

The Basement Membrane (BM) is a thin, specialized extracellular matrix structure that underlies epithelial and endothelial tissues throughout the body. Composed of various proteins, including collagen IV, laminins, nidogens, and proteoglycans, the BM serves as a critical scaffold for cell attachment and tissue organization. In addition to provide structural support, the BM plays essential roles in regulating cell behavior, migration, and signaling. Recent research has shed light on the mechanical properties of the BM and their significance in both physiological and pathological conditions. This article explores the mechanical properties of the basement membrane in health and disease, highlighting their implications for tissue function, homeostasis, and disease progression.

The basement membrane is a complex, multi-layered structure that separates epithelial and endothelial cells from underlying connective tissue. It is composed of several key components, including collagen IV, laminins, nidogens, and proteoglycans, each of which contributes to its unique mechanical properties.

Collagen IV is the most abundant protein in the basement membrane and forms a mesh-like network that provides tensile strength and stability. Laminins, a family of large glycoproteins, interact with collagen IV to anchor cells to the basement membrane and facilitate cell adhesion and migration. Nidogens act as bridging molecules, linking collagen IV and laminins to stabilize the basement membrane structure. Proteoglycans, such as perlecan, contribute to the hydrated gel-like matrix of the basement membrane, providing compressive strength and resilience.

Together, these components form a dynamic and adaptable scaffold that supports tissue integrity and function.

Mechanical properties of the basement membrane

The mechanical properties of the basement membrane are important for maintaining tissue architecture, providing mechanical support to cells, and transmitting forces within tissues. Several key mechanical properties contribute to the function of the basement membrane:

Elasticity: The basement membrane exhibits elastic behavior, allowing it to deform reversibly in response to mechanical stress. This elasticity is essential for tissue expansion and contraction, as well as for absorbing mechanical shocks and preventing tissue damage.

Stiffness: The stiffness of the basement membrane determines its resistance to deformation under load. Higher stiffness provides greater structural support but may also impede cell migration and tissue remodeling. Changes in basement membrane stiffness can alter cellular behavior and contribute to disease progression.

Viscoelasticity: The basement membrane displays viscoelastic properties, meaning it exhibits both elastic and viscous behavior. This allows it to absorb energy and dissipate mechanical forces over time, reducing the risk of tissue injury and promoting tissue resilience.

Adhesion strength: The basement membrane serves as a substrate for cell adhesion, providing anchorage points for cells to attach and spread. The strength of cell adhesion to the basement membrane influences cell migration, proliferation, and differentiation, as well as tissue morphogenesis and repair.

Role of mechanical properties in health and disease

In healthy tissues, the mechanical properties of the basement membrane are finely tuned to support tissue function and homeostasis. Proper basement membrane elasticity, stiffness, and viscoelasticity are essential for maintaining tissue integrity, facilitating cell migration and tissue repair, and regulating cell behavior and signaling. For instance, in the epithelial lining of blood vessels, the basement membrane provides structural support to endothelial cells and regulates vascular permeability and integrity. Changes in basement membrane mechanics can disrupt endothelial barrier function and contribute to vascular leakage and inflammation, as seen in diseases such as atherosclerosis and diabetes. Similarly, in the epithelial lining of

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Received: 20-Feb-2024, Manuscript No. JMST-24-25469; **Editor assigned:** 23-Feb-2024, Pre QC No. JMST-24-25469 (PQ); **Reviewed:** 08-Mar-2024, QC No. JMST-23-25469; **Revised:** 15-Mar-2024, Manuscript No. JMST-23-25469 (R); **Published:** 22-Mar-2024, DOI: 10.35248/2155-9589.24.14.381

Citation: Jorquera T (2024) The Role of Basement Membrane Mechanics in Health and Disease. J Membr Sci Technol. 14:381.

the lungs, the basement membrane supports alveolar epithelial cells and regulates gas exchange. Alterations in basement membrane stiffness can impair lung compliance and function, leading to respiratory diseases such as pulmonary fibrosis and Chronic Obstructive Pulmonary Disease (COPD). In the skin, the basement membrane anchors epidermal cells to the underlying dermis and regulates skin barrier function. Changes in basement membrane elasticity and adhesion strength can disrupt skin integrity and contribute to skin diseases such as eczema, psoriasis, and skin aging.

Dysregulation of basement membrane mechanics has been implicated in a wide range of diseases, including cancer, fibrosis, and inflammatory disorders. Changes in basement membrane elasticity, stiffness, and adhesion strength can alter cell behavior, promote tissue remodeling, and facilitate disease progression. In cancer, alterations in basement membrane mechanics can promote tumor invasion, metastasis, and angiogenesis. Increased basement membrane stiffness has been associated with tumor progression and poor prognosis in various cancers, including breast, lung, and pancreatic cancer. Tumor cells can remodel the basement membrane by secreting proteolytic enzymes and altering the expression of ECM proteins, leading to changes in basement membrane mechanics and promoting tumor invasion into surrounding tissues. In fibrosis, excessive deposition of ECM proteins, including collagen IV and laminins, can stiffen the basement membrane and impair tissue function. Increased basement membrane stiffness has been observed in fibrotic diseases such as liver fibrosis, kidney fibrosis, and pulmonary fibrosis, contributing to tissue dysfunction and organ failure. In inflammatory disorders, immune cells can interact with the basement membrane and ECM proteins, leading to changes in basement membrane mechanics and tissue inflammation. Basement membrane stiffness has been shown to regulate immune cell migration and activation in diseases such as rheumatoid arthritis, inflammatory bowel disease, and asthma.

CONCLUSION

The mechanical properties of the basement membrane plays an important role in maintaining tissue integrity, regulating cell behavior, and transmitting forces within tissues. Alterations in basement membrane mechanics can disrupt tissue homeostasis and contribute to the pathogenesis of various diseases, including cancer, fibrosis, and inflammatory disorders. Understanding the role of basement membrane mechanics in health and disease may provide new insights into disease pathogenesis and lead to the development of novel therapeutic strategies for treating a wide range of diseases. Further research into basement membrane mechanics and its therapeutic implications holds promise for improving patient outcomes and advancing the field of regenerative medicine.